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in Military Service Members

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<b>13. ABSTRACT (Maximum 200 Words)</b>  Background: In response to threats of bioterrorism, US military personnel began receiving smallpox vaccinations in 2003. Although some adverse health effects associated with smallpox vaccination are well described, much less has been documented about reproductive health outcomes. Smallpox vaccine, as a live-virus product, has caused fetal vaccinia in rare cases when given in pregnancy. The potential for the product to cause pregnancy loss, birth defects, or other birth problems has not been as well documented, especially in the recent era. Objectives: To describe the incidence and prevalence of adverse reproductive health outcomes among military service members who received smallpox vaccination. Research Methods: Electronic birth records are accessed directly from the Standard Inpatient Data Record (SIDR), Standard Ambulatory Data Record (SADR), Health Care Service Record (HCSR); immunization data are obtained from the Defense Eligibility and Enrollment System (DEERS). All data are accessed through formal agreements established by the DoD Birth and Infant Health Registry. Using these data, adverse reproductive health outcomes are assessed, including birth defects, pregnancy loss, and infertility among military families exposed to smallpox vaccine.				
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## INTRODUCTION

In response to perceived threats of biological weapons use by terrorists and rogue nations, the United States Food and Drug Administration (US FDA) approved the use of smallpox vaccine in October 2002. The US Department of Defense (DoD) established the Smallpox Vaccination Program for selected military personnel on 13 December 2002.(1) The vaccine approved by the FDA, Dryvax®, was first approved in 1931, and current stocks were produced by Wyeth Laboratories in the late 1970s to early 1980s. Because this vaccine was administered to billions of individuals over nearly half a century, the short-term adverse health events associated with the vaccine are fairly well documented.(2)

Although there is an adequate body of scientific literature on the adverse health effects associated with smallpox vaccination, much less has been reported concerning reproductive health. As a live virus product, smallpox vaccine has resulted in fetal vaccinia when given to pregnant women. This perinatal infection most often results in pregnancy loss or neonatal death; the risk of fetal vaccinia occurring after smallpox vaccination is estimated at 1/10,000 to 1/100,000.(3-7) No fetal vaccinia cases were observed among more than 4000 pregnant women vaccinated against smallpox in New York City in 1947.(8)

The risk of pregnancy loss, in the absence of fetal vaccinia, is less well established. While some large reviews reassure that no increased risk exists,(3,8,9) other small reports have cited concern that smallpox vaccination can cause spontaneous abortion.(10-12) Surveillance for pregnancy loss is always challenging because early pregnancies are difficult to recognize, losses may have multiple etiologies, and etiology is rarely established.(13-15) Likewise, risk factors for reduced fertility in relation to vaccination exposures can be extremely difficult to evaluate epidemiologically.(16-17) Large population-based studies, evaluating consistent and complete data sources are required to describe exposures associated with such outcomes.(18)

At least as concerning as pregnancy loss, an increased risk of birth defects can be extraordinarily alarming to prospective parents. Smallpox vaccination given during pregnancy has been associated with birth defects, specifically club foot malformations, in only one review in the 1970s.(19) These findings from Iran have been dismissed by many because they are not reproduced in other studies, and perhaps were associated with a vaccinia formulation that differs from the US Dryvax®.(20) Still others contend that live virus vaccines like smallpox, given during pregnancy, can plausibly cause birth defects.(21-24)

The risk for adverse reproductive health outcomes after exposures to non-pregnant women or men may be less biologically plausible than exposures to pregnant women, relying on delayed effects on germ cells. Given many unknowns about causation, the difference in plausibility does not necessarily make such exposures less concerning to families. Exposures associated with birth defects, in particular, remain an extraordinarily challenging issue for families, reproductive health researchers, and policymakers. In the US military, deployment to wars and associated military-unique exposures have caused great concern and resource-intensive research that assess later appearance of birth defects in children.(25-31)

Currently, with the exception of the passive Vaccine Adverse Events Reporting System (VAERS) for short-term outcomes,(32) there is no structured system to evaluate reproductive health effects of vaccinations.(33) The US military, charged with maintaining the health of all service members and their families, and with a growing population of women members,(34) has recently developed a strong surveillance system for birth defects.(35,36) This system has been applied in a judicious way to evaluate alleged associations between anthrax vaccination and birth defects, and has developed strong methodology and data validation protocols.(37,38) We are using this system to address the challenging questions surrounding potential associations between smallpox vaccine and adverse reproductive health outcomes.

## BODY OF REPORT

Methods are described in the protocol.

The project began and continues to collect and process both immunization and birth data. Immunization records have been extracted from the DEERS Active Duty Immunization datasets. These data are complete through

December 2003. In January 2005, the second in the series of seven extractions will be downloaded for the period 1 January through June 30, 2004.

Preliminary extractions have aggregated DoD dependent birth records for the Birth and Infant Health Registry from TriCare SIDR, SADR and HCSR tables through December 2003. The next scheduled extractions will occur in January 2005.

Results will be reported following data collection and analyses.

#### **KEY RESEARCH ACCOMPLISHMENTS**

Awaiting completion of data collection and analyses

#### **REPORTABLE OUTCOMES**

There are no reportable outcomes at this time.

#### **CONCLUSIONS**

Data collection continues. Analyses, results and conclusions are pending, as above.

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